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Olga M. Franz — Olga M Franz

Printed Name — Signature

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

The Accompanying Application

Applicants : Briner et al.

For : Aminoalkylbenzofurans: Serotonin Agonists

Docket No. : X-11594

ENTRY INTO U.S. NATIONAL PHASE UNDER PCT CHAPTER II

PRELIMINARY AMENDMENT PURSUANT TO 37 C.F.R. § 1.121 AND REMARKS PURSUANT TO 37 C.F.R. § 1.111

Assistant Commissioner for Patents

Washington, D. C. 20231

Sir:

This is a preliminary amendment accompanying a PCT Chapter II filing of PCT International Application No. PCT/US00/01342. Prior to examination of the above-identified application, entry of the following amendments is respectfully requested.

AMENDMENTS

IN THE CLAIMS:

Please amend claim 6 as follows:

6. (once amended) A method of [any of] Claim[s] 3[, 4, or 5] where the mammal is human.

Please add claims 7 and 8 as follows:

7. (new) A method of Claim 4 where the mammal is human;

8. (new) A method of Claim 5 where the mammal is human.

It is respectfully submitted that entry of the amendments submitted herewith introduce no new matter to the application. Claims 7 and 8 have been added to eliminate multiple dependencies. These amendments are not intended to affect the scope of the claims or limit the scope of the equivalents available to limitations thereof. A current set of all claims is attached herewith for the convenience of the Examiner.

It is respectfully submitted that the application is now in order for allowance.

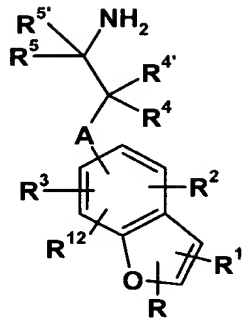
Respectfully submitted,

R. Craig Tucker
Attorney for Applicants
Registration No. 45,165
Phone: 317-433-9829

Eli Lilly and Company
Patent Division/DC1104
Lilly Corporate Center
Indianapolis, Indiana 46285

We Claim

1. The compounds of Formula I:



I

where:

A is $-CHR^{13}-$ or a bond;

R is hydrogen, halo, cyano, $-C(O)NR^6R^7$, C_1-C_6 alkyl, C_1-C_4 alkoxycarbonyl, carboxy, or phenyl optionally substituted with one or two substituents selected from the group consisting of halo, C_1-C_4 alkyl, and C_1-C_4 alkoxy;

R^1 is hydrogen, halo, cyano, carboxamido, formyl, trimethylsilyl, trifluoromethyl, pentafluoroethyl, or C_1-C_6 alkyl;

R^2 and R^3 are independently hydrogen, halo, amino, nitro, C_1-C_4 alkoxy, cyano, carboxamido, $-C(O)NR^8R^9$, $-NR^{10}R^{11}$, $-NHC(O)NHR^{14}$, C_1-C_4 alkoxycarbonyl, carboxyl, trifluoromethyl, or C_1-C_6 alkyl optionally substituted with a substituent selected from the group consisting of C_1-C_4 alkoxy, hydroxy, phenoxy, and phenyl;

R^4 and $R^{4'}$ are independently hydrogen, C_1-C_4 alkyl, or benzyl; or R^4 and $R^{4'}$ together with the carbon atom to which they are attached form a cyclopropyl moiety;

R^5 is hydrogen, C_1-C_4 alkyl, or benzyl;

$R^{5'}$ is hydrogen, or R^5 and $R^{5'}$ together with the carbon atom to which they are attached form a cyclopropyl moiety;

R^6 and R^7 are independently hydrogen or C_1-C_4 alkyl;

R^8 is hydrogen or C_1-C_4 alkyl;

R^9 is C_1-C_8 alkyl where the alkyl chain is optionally substituted with a substituent selected from the group consisting of carboxy, phenyl, or pyridyl, said phenyl or pyridyl substituent optionally substituted with one or two substituents selected from the group consisting of halo, C_1-C_4 alkyl, or C_1-C_4 alkoxy;

R^{10} is hydrogen or C_1-C_4 alkyl;

R^{11} is C_1-C_4 alkyl or C_1-C_4 acyl;

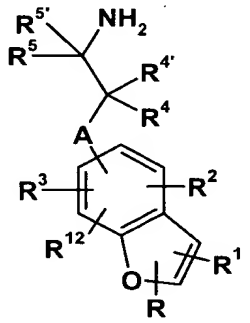
R^{12} is hydrogen, halo, or C_1-C_4 alkyl;

R^{13} is hydrogen, C_1-C_4 alkyl, or benzyl;

R^{14} is hydrogen, C_1-C_4 alkyl, or phenyl optionally substituted with a substituent selected from the group consisting of halo, C_1-C_4 alkyl, and C_1-C_4 alkoxy;

or pharmaceutically acceptable acid addition salts thereof.

2. A pharmaceutical formulation which comprises, in association with a pharmaceutically acceptable carrier, diluent or excipient, a compound of Formula I:



where:

A is $-CHR^{13}-$ or a bond;

R is hydrogen, halo, cyano, -C(O)NR^6R^7, C_1-C_6 alkyl, C_1-C_4 alkoxycarbonyl, carboxy, or phenyl optionally substituted with one or two substituents selected from the group consisting of halo, C_1-C_4 alkyl, and C_1-C_4 alkoxy;

R^1 is hydrogen, halo, cyano, carboxamido, formyl, trimethylsilyl, trifluoromethyl, pentafluoroethyl, or C_1-C_6 alkyl;

R^2 and R^3 are independently hydrogen, halo, amino, nitro, C_1-C_4 alkoxy, cyano, carboxamido, -C(O)NR^8R^9, -$NR^{10}R^{11}$, -NHC(O)NHR^{14}, C_1-C_4 alkoxycarbonyl, carboxyl, trifluoromethyl, or C_1-C_6 alkyl optionally substituted with a substituent selected from the group consisting of C_1-C_4 alkoxy, hydroxy, phenoxy, and phenyl;

R^4 and $R^{4'}$ are independently hydrogen, C_1-C_4 alkyl, or benzyl; or R^4 and $R^{4'}$ together with the carbon atom to which they are attached form a cyclopropyl moiety;

R^5 is hydrogen, C_1-C_4 alkyl, or benzyl;

$R^{5'}$ is hydrogen, or R^5 and $R^{5'}$ together with the carbon atom to which they are attached form a cyclopropyl moiety;

R^6 and R^7 are independently hydrogen or C_1-C_4 alkyl;

R^8 is hydrogen or C_1-C_4 alkyl;

R^9 is C_1-C_8 alkyl where the alkyl chain is optionally substituted with a substituent selected from the group consisting of carboxy, phenyl, or pyridyl, said phenyl or pyridyl substituent optionally substituted with one or two substituents selected from the group consisting of halo, C_1-C_4 alkyl, or C_1-C_4 alkoxy;

R^{10} is hydrogen or C_1-C_4 alkyl;

R^{11} is C_1-C_4 alkyl or C_1-C_4 acyl;

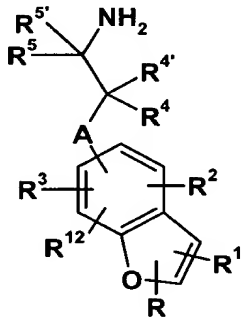
R^{12} is hydrogen, halo, or C_1-C_4 alkyl;

R^{13} is hydrogen, C_1-C_4 alkyl, or benzyl;

R^{14} is hydrogen, C_1-C_4 alkyl, or phenyl optionally substituted with a substituent selected from the group consisting of halo, C_1-C_4 alkyl, and C_1-C_4 alkoxy;

or pharmaceutically acceptable acid addition salts thereof.

3. A method for increasing activation of the 5-HT_{2C} receptor in mammals, comprising administering to a mammal in need of such activation a pharmaceutically effective amount of a compound of Formula I:



I

where:

A is -CHR^{13}- or a bond;

R is hydrogen, halo, cyano, -$C(O)NR^6R^7$, C_1-C_6 alkyl, C_1-C_4 alkoxycarbonyl, carboxy, or phenyl optionally substituted with one or two substituents selected from the group consisting of halo, C_1-C_4 alkyl, and C_1-C_4 alkoxy;

R^1 is hydrogen, halo, cyano, carboxamido, formyl, trimethylsilyl, trifluoromethyl, pentafluoroethyl, or C_1-C_6 alkyl;

R^2 and R^3 are independently hydrogen, halo, amino, nitro, C_1-C_4 alkoxy, cyano, carboxamido, -$C(O)NR^8R^9$,
-$NR^{10}R^{11}$, -$NHC(O)NHR^{14}$, C_1-C_4 alkoxycarbonyl, carboxyl, trifluoromethyl, or C_1-C_6 alkyl optionally substituted with a substituent selected from the group consisting of C_1-C_4 alkoxy, hydroxy, phenoxy, and phenyl;

R^4 and $R^{4'}$ are independently hydrogen, C_1-C_4 alkyl, or benzyl; or R^4 and $R^{4'}$ together with the carbon atom to which they are attached form a cyclopropyl moiety;

R^5 is hydrogen, C_1-C_4 alkyl, or benzyl;

$R^{5'}$ is hydrogen, or R^5 and $R^{5'}$ together with the carbon atom to which they are attached form a cyclopropyl moiety;

R^6 and R^7 are independently hydrogen or C_1-C_4 alkyl;

R^8 is hydrogen or C_1-C_4 alkyl;

R^9 is C_1-C_8 alkyl where the alkyl chain is optionally substituted with a substituent selected from the group consisting of carboxy, phenyl, or pyridyl, said phenyl or pyridyl substituent optionally substituted with one or two substituents selected from the group consisting of halo, C_1-C_4 alkyl, or C_1-C_4 alkoxy;

R^{10} is hydrogen or C_1-C_4 alkyl;

R^{11} is C_1-C_4 alkyl or C_1-C_4 acyl;

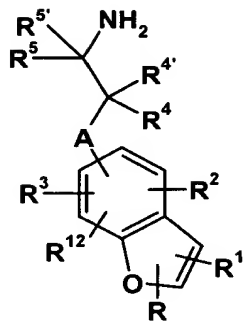
R^{12} is hydrogen, halo, or C_1-C_4 alkyl;

R^{13} is hydrogen, C_1-C_4 alkyl, or benzyl;

R^{14} is hydrogen, C_1-C_4 alkyl, or phenyl optionally substituted with a substituent selected from the group consisting of halo, C_1-C_4 alkyl, and C_1-C_4 alkoxy;

or pharmaceutically acceptable acid addition salts thereof.

4. A method for the treatment of obesity in mammals, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula I:



I

where:

A is $-CHR^{13}-$ or a bond;

R is hydrogen, halo, cyano, $-C(O)NR^6R^7$, C_1-C_6 alkyl, C_1-C_4 alkoxycarbonyl, carboxy, or phenyl optionally substituted with one or two substituents selected from the group consisting of halo, C_1-C_4 alkyl, and C_1-C_4 alkoxy;

R^1 is hydrogen, halo, cyano, carboxamido, formyl, trimethylsilyl, trifluoromethyl, pentafluoroethyl, or C_1-C_6 alkyl;

R^2 and R^3 are independently hydrogen, halo, amino, nitro, C_1-C_4 alkoxy, cyano, carboxamido, $-C(O)NR^8R^9$, $-NR^{10}R^{11}$, $-NHC(O)NHR^{14}$, C_1-C_4 alkoxycarbonyl, carboxyl, trifluoromethyl, or C_1-C_6 alkyl optionally substituted with a substituent selected from the group consisting of C_1-C_4 alkoxy, hydroxy, phenoxy, and phenyl;

R^4 and $R^{4'}$ are independently hydrogen, C_1-C_4 alkyl, or benzyl; or R^4 and $R^{4'}$ together with the carbon atom to which they are attached form a cyclopropyl moiety;

R^5 is hydrogen, C_1-C_4 alkyl, or benzyl;

$R^{5'}$ is hydrogen, or R^5 and $R^{5'}$ together with the carbon atom to which they are attached form a cyclopropyl moiety;

R^6 and R^7 are independently hydrogen or C_1-C_4 alkyl;

R^8 is hydrogen or C_1-C_4 alkyl;

R^9 is C_1-C_8 alkyl where the alkyl chain is optionally substituted with a substituent selected from the group consisting of carboxy, phenyl, or pyridyl, said phenyl or pyridyl substituent optionally substituted with one or two substituents selected from the group consisting of halo, C_1-C_4 alkyl, or C_1-C_4 alkoxy;

R^{10} is hydrogen or C_1-C_4 alkyl;

R^{11} is C_1-C_4 alkyl or C_1-C_4 acyl;

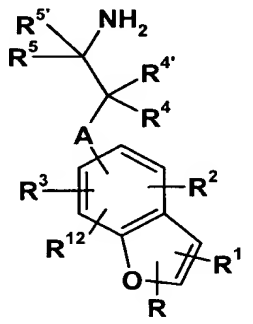
R^{12} is hydrogen, halo, or C_1-C_4 alkyl;

R^{13} is hydrogen, C_1-C_4 alkyl, or benzyl;

R^{14} is hydrogen, C_1-C_4 alkyl, or phenyl optionally substituted with a substituent selected from the group consisting of halo, C_1-C_4 alkyl, and C_1-C_4 alkoxy;

or pharmaceutically acceptable acid addition salts thereof.

5. A method for the treatment of depression in mammals, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula I:



I

where:

A is $-CHR^{13}-$ or a bond;

R is hydrogen, halo, cyano, $-C(O)NR^6R^7$, C_1-C_6 alkyl, C_1-C_4 alkoxycarbonyl, carboxy, or phenyl optionally substituted with one or two

substituents selected from the group consisting of halo, C_1-C_4 alkyl, and C_1-C_4 alkoxy;

R^1 is hydrogen, halo, cyano, carboxamido, formyl, trimethylsilyl, trifluoromethyl, pentafluoroethyl, or C_1-C_6 alkyl;

R^2 and R^3 are independently hydrogen, halo, amino, nitro, C_1-C_4 alkoxy, cyano, carboxamido, -C(O)NR^8R^9, -$NR^{10}R^{11}$, -NHC(O)NHR^{14}, C_1-C_4 alkoxycarbonyl, carboxyl, trifluoromethyl, or C_1-C_6 alkyl optionally substituted with a substituent selected from the group consisting of C_1-C_4 alkoxy, hydroxy, phenoxy, and phenyl;

R^4 and $R^{4'}$ are independently hydrogen, C_1-C_4 alkyl, or benzyl; or R^4 and $R^{4'}$ together with the carbon atom to which they are attached form a cyclopropyl moiety;

R^5 is hydrogen, C_1-C_4 alkyl, or benzyl;

$R^{5'}$ is hydrogen, or R^5 and $R^{5'}$ together with the carbon atom to which they are attached form a cyclopropyl moiety;

R^6 and R^7 are independently hydrogen or C_1-C_4 alkyl;

R^8 is hydrogen or C_1-C_4 alkyl;

R^9 is C_1-C_8 alkyl where the alkyl chain is optionally substituted with a substituent selected from the group consisting of carboxy, phenyl, or pyridyl, said phenyl or pyridyl substituent optionally substituted with one or two substituents selected from the group consisting of halo, C_1-C_4 alkyl, or C_1-C_4 alkoxy;

R^{10} is hydrogen or C_1-C_4 alkyl;

R^{11} is C_1-C_4 alkyl or C_1-C_4 acyl;

R^{12} is hydrogen, halo, or C_1-C_4 alkyl;

R^{13} is hydrogen, C_1-C_4 alkyl, or benzyl;

R^{14} is hydrogen, C_1-C_4 alkyl, or phenyl optionally substituted with a substituent selected from the group consisting of halo, C_1-C_4 alkyl, and C_1-C_4 alkoxy;
or pharmaceutically acceptable acid addition salts thereof.

6. (once amended) A method of [any of] Claim[s] 3[, 4, or 5] where the mammal is human[;]
7. (new) A method of Claim 4 where the mammal is human;
8. (new) A method of Claim 5 where the mammal is human.